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RESEARCH ARTICLE

A simple and sensitive electroanalytical determination of anxiolytic buspirone hydrochloride drug based on multiwalled carbon nanotubes modified electrode

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Abstract In the present study, a simple and sensitive buspirone hydrochloride (BPH) sensor was developed based on multiwalled carbon nanotubes (MWCNT) modified electrode. The modified electrode was characterized using transmission electron microscopy and electrochemical impedance spectroscopy. The MWCNT modified electrode showed an enhanced oxidation peak current response toward BPH than unmodified electrode. The oxidation peak potential of BPH at modified electrode was 0.85, which was quite lower than that of bare electrode (0.88 V). The BPH was successfully determined at modified electrode using different electrochemical methods, such as cyclic voltammetry (CV), differential pulse voltammetry (DPV), and amperometry. The good sensitivity and linear range response of BPH were obtained using amperometry when compared with other methods employed in this study (CV and DPV). The modified electrode displayed the electro-oxidation of BPH in the linear response from 0.5 to 99.5 μM with the sensitivity of 16.49 μA μM^{-1} cm^{-2}. The limit of detection was calculated as 0.22 μM. In addition, the modified electrode exhibited a good repeatability and repeatability with acceptable stability.

Keywords Multiwalled carbon nanotube · Buspirone hydrochloride · Oxidation · Electrochemical detection · Amperometry

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1 Introduction

Buspirone hydrochloride (BPH) is an anxiolytic drug, which is widely used for the treatment of anxiety disorder [1, 2]. The chemical structure of BPH is shown in Fig. 1. Nowadays, various methods have been employed for the accurate detection of BPH in the pharmaceutical field including high performance liquid chromatography (HPLC), differential pulse polarography, and calorimetric methods [3–6]. The aforementioned traditional methods are very sensitive and reliable, yet they consumed more time, cost, and also required many pretreatment procedures [7]. On the other hand, electrochemical methods have received considerable attention for detection of various pharmaceutical drugs owing to their simplicity with cost effectiveness [8–10]. Modified electrodes are playing an important role in the electrochemical analysis due to their good sensitivity and selectivity compared with bare electrodes [11]. Multiwalled carbon nanotubes (MWCNT) have exclusively used in the electroanalytical field due to its good electrical conductivity, mechanical strength, high surface area, and chemical stability. The special properties of MWCNT have been used for developing of various electrochemical sensors including the biological and drug molecules [12–14]. Since, the remarkable properties of MWCNT modified electrode have been widely used for sensitive detection of various pharmaceutical drugs [15–18]. However, only a few reports are available for the electrochemical detection of BPH using modified electrodes [19, 20]. To the best our knowledge, MWCNT modified electrode has not been used yet for electrochemical detection of BPH.

In this study, we report a simple and sensitive electroanalytical method for determination of BPH using MWCNT modified electrode. The modified electrode displayed an enhanced oxidation peak for BPH when

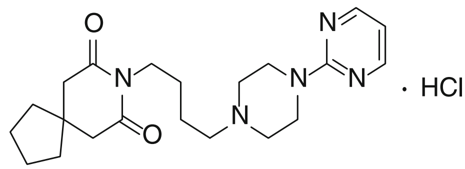


Fig. 1 The chemical structure of buspirone hydrochloride

compared with unmodified electrode. The BPH was successfully determined by using cyclic voltammetry (CV), differential pulse voltammetry (DPV), and amperometry. In addition, the practicality of the proposed sensor was evaluated in commercially available BPH tablets.

2 Experimental

2.1 Materials

Buspirone hydrochloride (BPH) was purchased from Sigma Aldrich. MWCNTs with the lengths of 0.1–10 μm were obtained from Aldrich. The commercial BPH tablets were obtained from the local drug store in Madurai, Tamilnadu, India. Dopamine (DA), ascorbic acid (AA), and uric acid (UA) were purchased from Aldrich. The supporting electrolyte used for all experiments was pH 7.0 phosphate buffer solutions (PB), which was prepared by using 0.05 M Na_2HPO_4 and NaH_2PO_4 solutions with doubly distilled water. All the other pH solutions were adjusted with 0.5 M H_2SO_4 and 2 M NaOH. All the reagents used for the preparation of solutions were of analytical reagent grade and used without any further purification.

For real sample analysis, commercially available BPH tablets (5 mg LC) were used. Prior to the analysis, the mortar and pestle were cleaned with distilled water for several times after that the 20 tablets were crushed into very fine powder. For the preparation of 0.005 M concentration of BPH real sample, the crushed tablet powder was accurately weighed and transferred into 25 ml volumetric flask, 10 ml of pH 7 (0.05 M PB) solution was added followed by ultra sonication in cold water bath about 25 min, finally the solution was made up to 25 ml mark with the buffer solution.

2.2 Methods and electrode fabrication

A CHI 1205 electrochemical workstation (CH Instruments) was employed for the cyclic voltammetry (CV), and differential pulse voltammetry (DPV) were performed using CHI 750a work station. The surface morphology of the modified electrode was investigated by transmission electron microscopy (TEM), and it was performed by using JEM 2007 model transmission electron microscope. Electrochemical impedance spectroscopy (EIS) studies were performed by using IM6ex ZAHNER (Kroanch, Germany). Amperometric (*i*–*t* curve) measurements were performed using a CHI-750a potentiostat with an analytical rotator AFMSRX (PINE instruments, USA). The construction of a electrochemical cell which contains a conventional three-electrode system consisting of a modified glassy carbon electrode (GCE) was used as the working electrode (active surface area = 0.079 cm^2), an Ag/AgCl electrode (Sat. KCl) as the reference electrode, and a platinum wire with 0.5 mm diameter as the counter electrode was employed for the entire electrochemical experiments in this study. All of the experiments were carried out at ambient temperature, and solutions in the electrochemical cell were kept under oxygen-free atmosphere.

Prior to modification, GCE was polished with alumina slurry and slightly sonicated for about 3 min in water and ethanol (1:1) mixture. MWCNT (0.1 g/mL) was dispersed well in dimethylformamide (DMF) with the aid of sonication for 90 min. About 6 μL of MWCNT (optimized concentration) was carefully drop cast onto the precleaned GCE and dried at room temperature for a few minutes. Finally, MWCNT modified GCE was used for further experiments and stored in room temperature under dry condition when not in use.

3 Results and discussions

3.1 Electrochemistry of BPH at MWCNT modified electrode

Cyclic voltammetry was employed to evaluate the electrochemical behavior of BPH at MWCNT modified electrode in deoxygenated PB. Figure 2 shows the CVs of bare (a) and MWCNT (b) modified GCEs in the presence of 33 μM BPH at the scan rate of 100 mVs^{-1}. CVs were recorded in the potential range of 0.6–1.2 V. A well defined oxidation peak appeared at the potential of 0.85 V attributed for the oxidation of BPH at MWCNT modified electrode. The oxidation peak accredited to the oxidation of BPH to protanated buspirone [21]. The oxidation peak of BPH appeared at 0.88 V at bare GCE. Moreover, the oxidation peak current (I_{pa}) of BPH is relatively small when compared with MWCNT modified electrode. The modified electrode displayed fivefold enhanced I_{pa} with lower oxidation peak potential (0.85 V) for BPH than unmodified electrode. The enhanced I_{pa} attributed to the high surface area and good biocompatibility of MWCNT modified electrode.

The oxidation mechanism of BPH has not been reported yet. Generally, the reduction of BPH occurred at high negative potentials (−1.4 V), and oxidation was occurred at positive potentials (0.85 V). We believe that the oxidation of BPH takes place in the nitrogen present nearby the

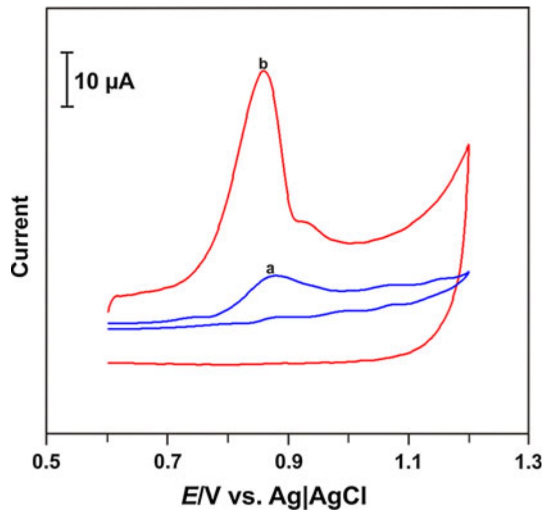


Fig. 2 Cyclic voltammetry response for Bare (*a*) and MWCNT modified GCEs (*b*) in the presence of 33 μM BPH in deoxygenated PB at 100 mVs^{-1} scan rate

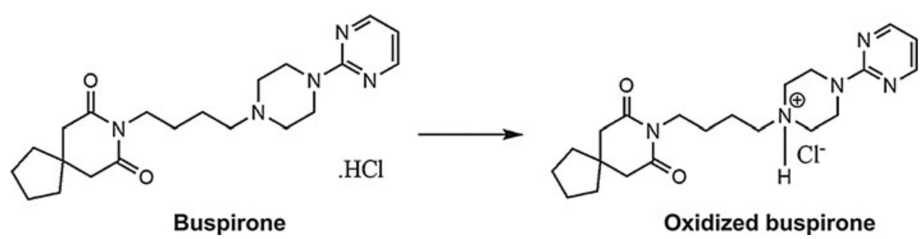
aliphatic chain, while the possibility of oxidation of other nitrogen is quite difficult due to the presence of bulky groups. The typical oxidation mechanism of BPH at MWCNT modified electrode is shown in Fig. 3.

3.2 Effect of scan rate and pH

Figure 4A shows the cyclic voltammograms obtained at MWCNT modified GCE in deoxygenated PB containing 15 μM BPH at various scan rates. Upon increasing the scan rates, the oxidation peak current of BPH increased linearly. Meanwhile, oxidation peak also shifted toward the positive direction. The oxidation peak current was linearly increased with the scan rates ranging from 50 to 500 mVs^{-1} (Fig. 4A inset). The peak potentials shifted toward a positive direction at higher scan rates, suggesting that BPH oxidation at MWCNT/GCE modified electrode is characteristic of a typical adsorption controlled process.

The influence of pH related to the oxidation peak current (I_{pa}) and peak potential (E_{pa}) of BPH was studied at MWCNT modified electrode and shown in Fig. 4B. The effect of pH was studied in various buffer solutions (pH 11–4) at 100 mVs^{-1}. The maximum I_{pa} was observed at pH 7 when compared with other pH solutions. Since the maximum I_{pa} of BPH appeared at pH 7, so pH 7 buffer solution was used throughout the experiments. Moreover, E_{pa} of BPH has a linear dependence over the pH ranging from 4 to 9 with the correlation coefficient of 0.980 (inset). This result further validates that the electro-oxidation of

Fig. 3 A typical electro-oxidation mechanism of BPH at MWCNT modified electrode



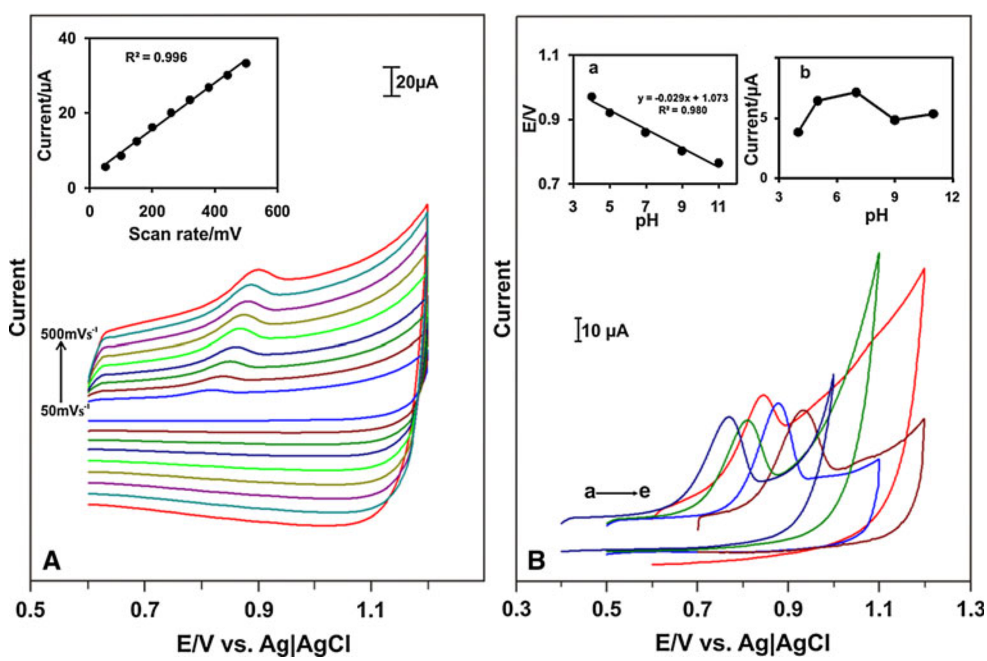


Fig. 4 **A** Cyclic voltammograms recorded at MWCNT modified electrode in 15 μM BPH in deoxygenated PB at different scan rates. *Inset* shows the linear dependence of I_{pa} vs. scan rate (50–500 mV s^{-1}). **B** Cyclic voltammograms obtained at MWCNT modified GCE in 37.5 μM BPH in deoxygenated various buffer solutions [(*a*) pH-11, (*b*) pH-9, (*c*) pH-7, (*d*) pH-5, and (*e*) pH-4] at the scan rate of 100 mVs^{-1}. *Inset* shows E_{pa} vs. pH (*a*) and I_{pa} vs. pH (*b*)

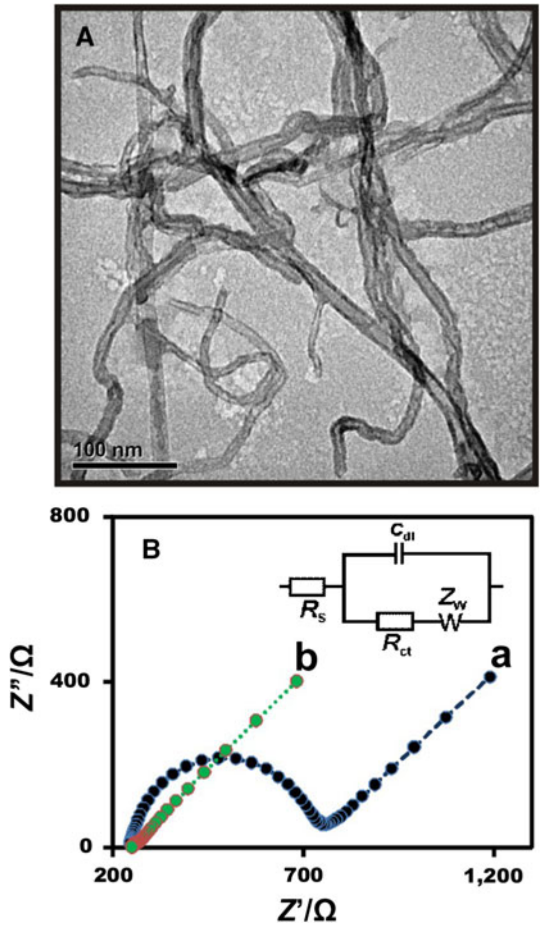


Fig. 5 **A** A typical TEM image of MWCNT. **B** EIS of bare (*a*) and MWCNT modified GCEs (*b*), in 5 mM $Fe(CN)_6^{3-/4-}$ containing 0.1 M KCl. *Inset* is the Randles equivalent circuit. R_s, C_{dl}, R_{ct}, and Z_w represent the resistance of the electrolyte solution, double layer capacitance, charge–transfer resistance, and the Warburg impedance, respectively. The frequency range is from 0.1 Hz to 100 kHz

BPH at MWCNT modified electrode is pH dependent reaction.

3.3 Characterization of the modified electrode

The modified electrode was characterized using TEM and EIS analysis. Figure 5A shows a typical TEM image of the MWCNT modified electrode. It can be clearly seen that, MWCNTs were clearly observed like tubular structures with an average diameter of 30–50 nm. The rough surface area of MWCNT that easily allows BPH to be adsorbed effectively on MWCNT, resulting in the efficient electron transfer of BPH and more favorable for the oxidation of BPH toward the electrode surface. The electrochemical impedance behaviors of different modified electrodes were studied by using EIS analysis. Figure 5B shows typical EIS of the real and imaginary parts of the impedance spectra represented as Nyquist plots (Z_{im} vs. Z_{re}) of Bare (a) and MWCNT (b) modified GCEs in PB containing 5 mM $Fe(CN)_6^{3-/}Fe(CN)_6^{4-}$. From the Randles equivalence circuit model (inset), we have calculated the electron transfer resistance (R_{et}) values of each modified electrode and the frequency range set from 0.1 Hz to 100 kHz. Generally, a semicircle portion of the Nyquist plot results from the parallel combination of R_{et} and C_{dl} resulting from electrode impedance. The EIS of bare GCE exhibits a larger semicircle part with the R_{et} value of 468.5 Ω, whereas depressed semicircle with smaller diameter was observed for MWCNT modified electrode ($R_{et} = 9.9$ Ω). This result clearly indicates that the faster electron transfer occurs at MWCNT modified electrode rather than bare GCE. The low resistance of MWCNT modified electrode is attributed to the excellent conductivity and good compatibility of MWCNT networks.

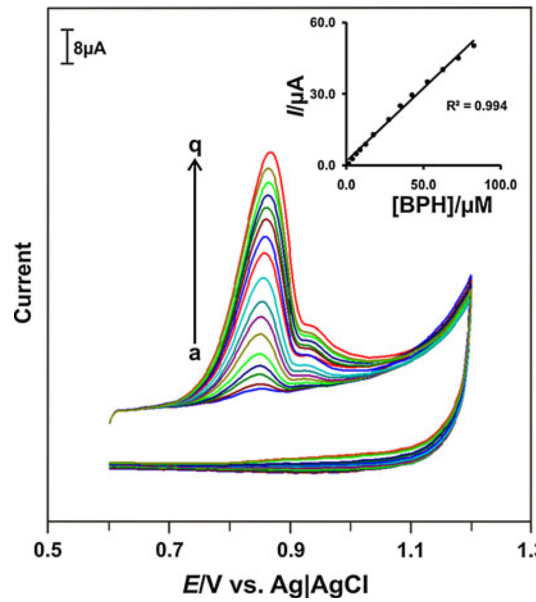


Fig. 6 Cyclic voltammograms obtained at MWCNT modified electrode for 1.5–83 μM (*a*–*q*) of BPH in PB at 100 mV s^{-1} scan rate. *Inset* plot shows the linear dependence of I_{pa} vs. [BPH]

3.4 Cyclic voltammetry

Figure 6 shows the cyclic voltammograms of MWCNT modified electrode in the presence of different concentrations of BPH in PB (pH 7). In the presence of BPH, a good oxidation peak was appeared at 0.85 V. Upon increasing the concentration, the oxidation peak current increased gradually up to 83 μM. Moreover, the oxidation peak current is increased linearly with successive addition of different concentrations of BPH (a–q). Furthermore, from the calibration curve, the linear range was found for BPH from 1.5 to 83 μM with a correlation coefficient of 0.994 (inset). The limit of detection (LOD) was found to be 0.23 μM based on a signal-to-noise ratio of 3. The sensitivity was calculated to be 7.775 μAμM^{-1} cm^{-2} ($N = 3$).

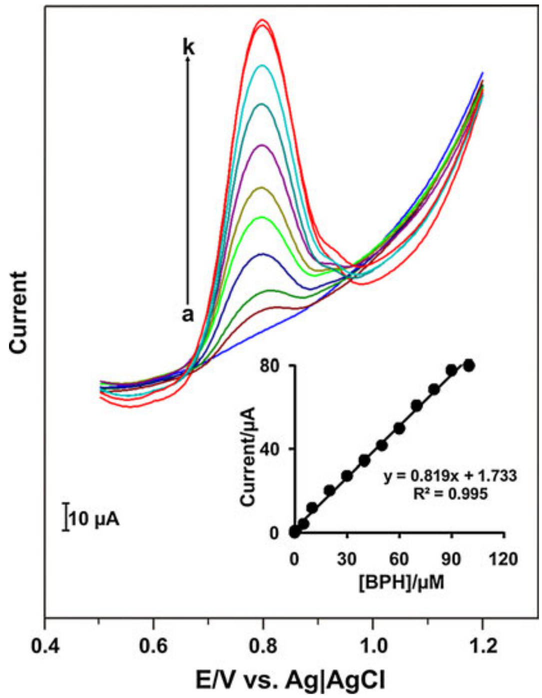


Fig. 7 DPVs recorded at MWCNT modified GCE (*a*) without and (*b*–*k*) with 0.3 µM–90.3 µM of BPH containing deoxygenated PB at 100 mV s^{-1} scan rate. Inset plot shows the linear dependence of I_{pa} vs. [BPH]

3.5 Differential pulse voltammetry

DPV were performed for the determination of BPH at MWCNT modified electrode in the potential range of 0.5–1.2 V at the scan rate of 100 mVs^{-1} shown in Fig. 7. A well-defined anodic peak response was observed at 0.81 in the presence of BPH. Moreover, the oxidation peak current of BPH increased linearly with increasing BPH concentrations ranging from 0.3 to 90.3 µM (inset) with the correlation coefficients of 0.995. The sensitivity was calculated as 10.36 $\mu A \mu M^{-1}$ cm^{-2} ($N = 3$). The LOD was found to be 0.18 µM with the RSD of 3.78 ($N = 3$). This result further confirmed that DPV is a quite sensitive method for the determination of BPH than CV method.

3.6 Amperometry

We used amperometric i–t method to evaluate the performance of the proposed sensor, which is more reliable and sensitive technique when compared with other techniques. We used the rotating ring disc (active surface area = 0. 24 cm^2) electrode for the amperometric measurements. During the amperometric *i*–*t* measurements, the electrode potential was held at 0.81 V (from the DPV) in the constantly stirred N_2 saturated PB (pH 7). For every 50 s, aliquots of different concentrations of BPH were injected into the constantly stirred PB solution. Figure 8A shows the typical amperometric *i*–*t* response obtained at MWCNT modified rotating disc GCE (surface area = 0.24 cm^{-2}) upon various BPH concentration additions. The response time of the proposed sensor was calculated as ~6 s, validating the rapid oxidation of BPH occurring at the modified electrode surface. The oxidation current increased linearly with increasing BPH concentrations in the range of 0.5–99.5 µM with the correlation coefficients of 0.994 (inset). The LOD was calculated to be 0.22 µM. Moreover, the proposed sensor showed a sensitivity of 16.49 µA μM^{-1} cm^{-2}. The various electroanalytical determinations of the BPH at MWCNT modified electrode are shown in Table 1. It can be seen from the Table 1 that the amperometric method is highly sensitive one for determinations of BPH than other electroanalytical methods (CV and DPV) used in this study. The comparison of the analytical performance of our BPH sensor has been compared with previously reported other traditional methods and the results have been provided in Table 2. It can be seen from Table 2 that our electrochemical method is comparable with previously reported traditional techniques. However, the demonstrated electroanalytical method is simple and inexpensive one when compared to the traditional methods employed for BPH determination [20, 22–24].

3.7 Selectivity studies

The selectivity of the modified electrode was investigated by using an amperometric *i*–*t* technique and shown in Fig. 8B. The experimental conditions are same as like Fig. 8A. The selectivity studies were carried out using 10 µM BPH in the presence of each addition of 50 µM of DA (b), AA (c), UA (d) at different time intervals into constantly stirred N_2-saturated PB (pH 7). The tolerance levels of the each suspicious species are quite negligible compared with a response of 10 µM BPH. The results clearly validate that the proposed electrode holds good selectivity for the determination BPH in the pharmaceutical formulations.

3.8 Stability, repeatability and reproducibility

In order to investigate the storage stability of the modified electrode, it was stored in pH 7 solution containing 53 µM BPH at 4 °C, and its background current was tested periodically for 20 h. The modified electrode retains 95.2 % of its initial sensitivity, indicating the good storage stability of the proposed sensor. The repeatability and reproducibility of the proposed sensors were evaluated by CV studies. The five electrodes fabricated independently with three different sets of measurements showed an acceptable reproducibility with a relative standard deviation (RSD) of 2.04 % for each 53 µM BPH concentration. The RSD for each 53 µM BPH measurements ($n = 10$) was 1.77 % revealing

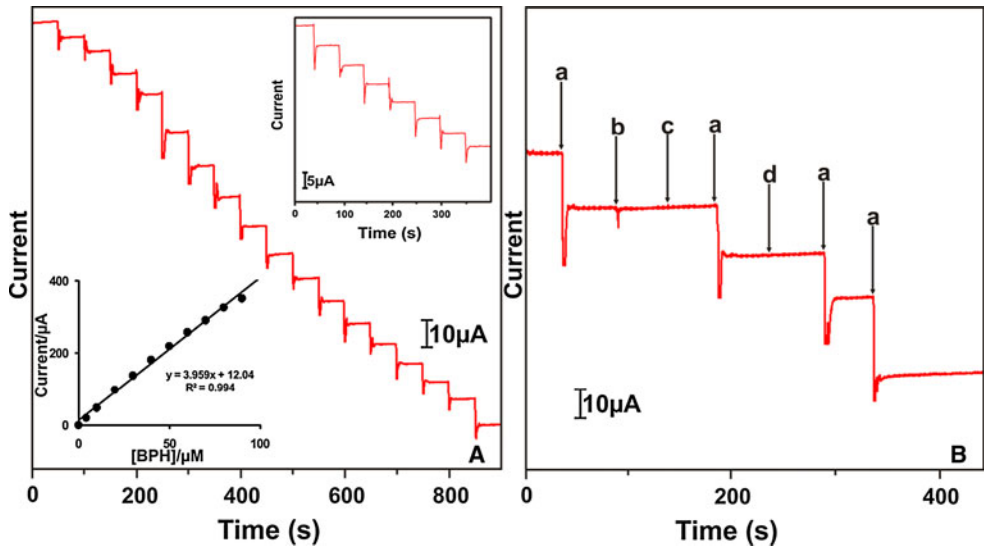


Fig. 8 **A** Amperometric *i*–*t* response at MWCNT modified rotating disc GCE upon successive additions of 0.5 μM–99.5 μM of BPH into continuously stirred N_2 saturated PB. Applied potential: 0.81 V; *Inset* (below) plot shows the calibration curve of [BPH] versus current response and *inset* (*above*) amperometric response for each addition of 2 μM BPH. **B** Amperometric responses acquired under similar conditions for successive addition of 10 μM BPH (*a*), 50 μM of DA (*b*), AA (*c*), and UA (*d*)

Table1 Determination of BPH at MWCNT modified electrode by using different electrochemical methods

Method	Sensitivity (μA μM^{-1} cm^{-2})	LOD (μM)	Linear range (μM)
CV	7.775	0.23	1.5–83.0
DPV	10.36	0.18	0.3–90.3
Amperometry	16.49	0.22	0.5–99.5

LOD Limit of detection

the good repeatability of the proposed electrochemical sensor.

3.9 Practicality

The real sample analysis is very important to evaluate the practicability of the modified electrode. The real sample analysis was carried out by using an amperometric *i*–*t* technique similar like Sect. 3.6. The analytical performances of the modified electrode were summarized in Table 3. It was evident that the modified electrode possessed good recovery results toward commercially available BPH tablets. The good recovery result indicates the proposed electrode could be effectively used for real time sensing of BPH in pharmaceutical formulations.

Table3 Determination of BPH in a pharmaceutical sample using amperometric method

Sample labeled	Added (μM)	Found (μM)	Recovery (%)
1	25	24.18	96.7
2	50	49.78	99.6
3	75	75.18	100.2

4 Conclusion

A simple electrochemical method was used for the determination of BPH based on MWCNT modified electrode. The BPH was effectively determined by using different electroanalytical methods like CV, differential pulse voltammetry (DPV), and amperometry. The MWCNT modified electrode showed enhanced oxidation peak current response for BPH than unmodified electrode. The proposed electrode holds an acceptable linear range of detection for BPH with good sensitivity. Moreover, modified electrode

Table 2 Comparison of the analytical parameters of the proposed method with other existing traditional methods for BPH determination

Method used	Linear response	LOD	Reference
Absorptive voltammetry	Up to 5 μM	0.005 μM	20
HPLC	0.5–10 *ng* mL^{-1}	0.5 *ng* mL^{-1}	22
Adsorptive stripping voltammetry	1–30 *ng* mL^{-1}	0.20 *ng* mL^{-1}	23
Mass spectrometry	0.025–10 *ng* mL^{-1}	0.025 *ng* mL^{-1}	24
Amperometry	0.5 – 99.5 μM	0.22 μM	Present study

LOD Limit of detection

HPLC High performance liquid chromatography

was highly selective and sensitive for BPH. Moreover, the best recovery results of the fabricated electrode in BPH tablets, indicating good practicability. As a future prospective, this BPH sensor can be used as a promising material for the determination of BPH in the pharmaceutical fields in the near future.

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